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INCIDENCE OF TESTICULAR CANCER IN U.S. AIR FORCE OFFICER AVIATORS: 1998-2008

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This report documents the results of a research project looking at the association between U.S. Air Force (USAF) aviators and the diagnosis of testicular cancer. The research was performed as a retrospective cohort study. The results of the study showed an association between USAF aviation and being diagnosed with testicular cancer. The testicular cancer incidence rate was 16.9 cases/100,000 in USAF male aviators and 7.8 cases/100,000 in USAF male nonaviators. USAF male aviators have a relative risk of 2.15 for being diagnosed with testicular cancer when compared to their nonaviator colleagues.

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1.0 SUMMARY

This report documents the results of a research project looking at the association between U.S. Air Force (USAF) aviators and the diagnosis of testicular cancer. The research was performed as a retrospective cohort study. The results of the study showed an association between USAF aviation and being diagnosed with testicular cancer. The testicular cancer incidence rate was 16.9 cases/100,000 in USAF male aviators and 7.8 cases/100,000 in USAF male nonaviators. USAF male aviators have a relative risk of 2.15 for being diagnosed with testicular cancer when compared to their nonaviator colleagues.

2.0 BACKGROUND

Cancer was the second leading cause of death in the United States in 2007, trailing only heart disease. Just over a half million Americans died from cancer in 2007 (Ref 1). In 2007, there were 7,765 cases of testicular cancer reported in the U.S. Although rare, testicular cancer is the most common cancer diagnosed in the American male population between the ages of 15 and 34. The overall incidence rate for testicular cancer was 5.5 cases per 100,000 males. In the population under the age of 65, the incidence rate was 6.1 cases per 100,000 males, while in the population aged 65 and over the incidence rate was 1.1 cases per 100,000 males (Ref 2). These data illustrate the fact that this is a cancer that primarily affects a younger population. This population tends to be the group that is in its wage-earning period of life; thus, this cancer has a significant impact. This is also the population that makes up the majority of our military, so this cancer also has an impact on our military forces. On a more positive note, testicular cancers have a 5-yr survival rate over 99% and 95% for localized tumors and tumors that have spread to regional lymph nodes, respectively. For tumors that have metastasized, the 5-yr survival rate is 71.5%. Most testicular tumors are detected at an early stage; thus, the mortality rate from testicular cancer is relatively low at 0.2 annual deaths per 100,000 men (Ref 2).

Testicular cancers can be divided into germ cell tumors and nongerm cell tumors. Germ cell tumors are by far the most common of the testicular cancers, accounting for almost 95% of all testicular tumors (Ref 3). Germ cell tumors can be classified as seminomas and nonseminomas. Seminomas account for approximately one-half of all germ cell tumors. Nonseminomas are inclusive of many histologic types including embryonal carcinoma, teratoma, choriocarcinoma, yolk-sac tumors, and mixed germ cell tumors. There is a wide variety of tumors that make up the 5% of testicular tumors that are not germ cell tumors. These include sex cord stromal tumors (Leydig cell tumors, Sertoli cell tumors, and granulose cell tumors), mixed germ cell and stromal tumors (gonadoblastoma), adnexal and paratesticular tumors (mesothelioma and adenocarcinoma of the rete testis), and other miscellaneous neoplasms (carcinoid, lymphoma, and cysts).

Several risk factors have been linked to testicular cancer. Cryptorchidism is the condition where one or both testicles fail to descend into the scrotum at the appropriate time. This condition has been shown to have a relative risk of 7.5 for developing testicular cancer when compared to men who did not have cryptorchidism (Ref 4). There is an increased incidence rate in white men when compared to black men. It has also been demonstrated that there are certain geographic areas that have higher incidence rates, with Scandinavian countries having the highest rates, the United States having a slightly lower rate, and African countries having a very

low rate (Ref 5). Testicular cancers have also been found more commonly in those men who come from a higher socioeconomic level (Ref 6).

Several occupational exposures have been studied and found to be associated with increased incidence rates of cancer, in particular testicular cancer. Polyvinyl chloride exposure has been linked to an increased odds ratio (OR) of being diagnosed with testicular cancer (Ref 7). Another study demonstrated an increased OR for developing testicular cancer when the exposure to low-frequency magnetic fields was increased (Ref 8). Exposure to occupational radiation has been linked to an increased relative risk of several cancers including testicular cancer in men (Ref 9).

Exposure to ionizing radiation in the aviation cohort has been examined many times as a potential occupational hazard that can lead to increased cancer rates. The results of these studies, when looking specifically at testicular cancer, have not been consistent (Ref 10). Band and colleagues found an increase of the standardized incidence rate (SIR) for testicular cancer of 1.75. This was based upon two cases of seminomas diagnosed in a cohort of Canadian civilian airline pilots. This result, while suggestive of an association, was not found to be statistically significant because of the small number of cases (Ref 11). Haldorsen and colleagues found a similar result when they looked at cancer incidence rates among Norwegian airline cabin attendants. An increased SIR for testicular cancer of 1.5 was noted for the small number of men in this cohort. Once again, because of the small number of cases, this result was not found to be statistically significant (Ref 12). Irvine and Davies studied the mortality of British Airways pilots and found a significantly elevated proportional mortality ratio for all cancers of 1.31. Colon cancer, brain cancer, and malignant melanoma were all found to have increased mortality ratios when compared to the general population mortality rates, but testicular cancer was not noted to have an increased mortality ratio in this study (Ref 13). In a study of Swedish civilian airline cabin crew, Linnersjo and colleagues did not find an increased testicular cancer incidence rate (Ref 14). In a cohort study of pilots in five Nordic countries that included over 10,000 male pilots, Pukkala and colleagues found that there was just a small, not statistically significant, elevation in the SIR for all cancers. When looking specifically at testicular cancer, the SIR was 0.94, indicating that there were fewer observed testicular cancer cases in pilots than were expected (Ref 15). Interestingly, in a previously published study using the same cohort, Pukkala and colleagues reported an SIR for testicular cancer of 1.11. This was not a statistically significant result. Looking at the methods for these studies, it is difficult to explain this apparent contradiction (Ref 16). In a study of mortality in a large cohort of airline cabin attendants in Europe, Zeeb and colleagues did not report an increased mortality due to testicular cancer (Ref 17). All of these studies evaluated civilian aviation cohorts and compared the aviation cancer rates to the rates in the general population. There have been several studies that determined the testicular cancer rates in military pilots. These studies have an advantage in that they used a comparison population of nonaviation military officers that was from a comparable socioeconomic class. In a study of morbidity in U.S. Navy aviators, Hoiberg and Blood found a significantly elevated risk of testicular cancer in U.S. Navy aviators when compared to nonaviators (Ref 18). Grayson and Lyons studied cancer incidence rates in U.S. Air Force (USAF) aviators using hospital discharge data and found a testicular cancer incidence relative risk of 1.69 when comparing aviators with nonaviators (Ref 19).

This study sought to determine if there was an increased incidence of testicular cancer in USAF officers who were also aviators when compared to USAF officers who were not aviators. This would allow for a comparison of populations with similar socioeconomic demographics.

This study did not attempt to identify specific factors that might have contributed to increased risk of testicular cancer in military aviators, but it would identify if there is an association between aviation careers and testicular cancer that needs further study. This study differed from the previous USAF study in that it used a different database and it looked at odds ratios when comparing the groups rather than at standardized incidence rates and risk ratios.

3.0 MATERIALS AND METHODS

The use of subjects in this research was compliant with the requirements for waiver of consent under 32 CFR 219 and AFI 4-402.

This study was designed as a retrospective cohort study. The cohort that was studied was men on active duty in the USAF between 1998 and 2008. The outcome of interest was the diagnosis of testicular cancer. The exposure variable that was examined in this study was the presence or absence of military flight hours. Those men with military flight hours were considered aviators for this study. After the study design was approved by the appropriate Institutional Review Board, data on testicular cancer were obtained using the Automated Central Tumor Registry (ACTUR) database. ACTUR was established in 1986 by the Department of Defense (DoD) to serve as a comprehensive cancer data reporting system for military beneficiaries. ACTUR was initially designed as a multihospital data collection system but was modified in 1998 to become a more inclusive central registry as the DoD moved away from maintaining hospitals to more clinic-based health care delivery. A query was run in ACTUR to create a database containing all of the entries that listed testicular cancer as the primary cancer. The ACTUR data were inclusive of all DoD beneficiaries but were then limited to USAF officers for the purpose of this study. ACTUR can contain duplicate entries, which were reduced to single entries. Using the list of USAF officers diagnosed with testicular cancer, the Air Force Personnel Center (AFPC) was queried as to the total flight hours and Air Force Specialty Code (AFSC) for these individuals. For the purpose of this study, the line of demarcation between flyers and nonflyers was documentation of any flight hours. The AFPC data revealed that some of the individuals on the list were enlisted personnel, so these individuals were removed from the analysis. The ACTUR data and the AFPC data were then combined to provide the final database that included cancer data as well as flight hours and AFSC information. Because of the change in the ACTUR database in 1998, the final analysis was limited to those diagnosed with testicular cancer between 1998 and 2008.

To get incidence rates, the population at risk needed to be determined. This was accomplished using the AFPC Retrieval Application Website (RAW). RAW is a website that provides accurate personnel statistics for the USAF. Currently, the RAW system can only be accessed by military members or Title 5 Civil Service employees through a .mil/.gov domain, and DoD security protocols apply. The same information would be available to the general public through the Interactive Demographic Analysis System provided by AFPC. The total number of male officers on active duty as well as those who were on flying status was obtained for every year from 1998 to 2008. Officers were considered to be aviators based upon their Rated Position Identification (RPI). The RPI is a USAF personnel classification system used to identify those who are in flying positions. Those with an RPI of 1 (pilots), 2 (navigators), 5 (flight surgeons), 6 (staff positions, wing or below, flying), 7 (flying position, not with USAF), and 8 (staff position, above wing, flying) were included in the population of flyers. The

population of nonflyers was calculated by subtracting the total population of flyers from the total population of officers for the given year.

Testicular cancer incidence rates were calculated individually for each year from 1998 to 2008, and then an overall rate for the inclusive period was calculated. This was done for those classified as aviators as well as for the nonflyers. A paired Student's t-test was performed on the yearly testicular cancer incidence rates in aviators and nonaviators to see if there was a significant difference. The relative risk for developing testicular cancer for aviators compared to nonaviators was then calculated. Statistical analysis was calculated using Excel 2007 (Microsoft Corp., Redmond, WA).

4.0 RESULTS

Analysis of the data indicated that there were 63 cases of testicular cancer diagnosed in our study population between 1998 and 2008. Of these cases, 25 were in men classified as aviators and 38 were in nonaviators. The average age at diagnosis for aviators was 33.5, with a range of 22 to 50 years. The average age at diagnosis for nonaviators was 35.9, with a range of 20 to 63 years (Table 1).

Table 1. Testicular Cancer Case Demographics for USAF Active Duty Officers, 1998-2008

Group	Cases	Age (yr)		
		Average	Minimum	Maximum
Aviators	25	33.5	22	50
Nonaviators	38	35.9	20	63
Total	74	35.1	20	63

There was a wide range of flight exposure for those classified as aviators as evidenced by the wide range of military flight time recorded by AFPC. The average flight time was 843.0 h with a range of 5.3 h to 3971.0 h. The median number of flight time hours was 225.1.

The number of cases diagnosed in the aviator group in any given year ranged between 0 and 5, resulting in an annual rate for testicular cancer for aviators ranging between 0.0 and 37.0 cases per 100,000 population. The number of cases diagnosed in the nonaviator group in any given year ranged between 1 and 7, resulting in an annual rate for testicular cancer for nonaviators ranging between 2.2 and 15.5 cases per 100,000 population. When all of the years were combined, the rate of testicular cancer among aviators was 16.9 cases per 100,000 population. The rate for nonaviators was 7.8 cases per 100,000 population. When looking at the two groups combined, there were 63 cases in a population of 632,323, giving an overall rate of testicular cancer for men on active duty in the USAF of 10.0 per 100,000 population (Table 2). The paired Student's t-test had a statistically significant result ($p = 0.034$) when comparing the yearly incidence rates in aviators with nonaviators.

When comparing the overall aviation to nonaviation testicular cancer rates, there is a relative risk of being diagnosed with testicular cancer of 2.15 (95% confidence interval 0.67-6.89). This indicates that the chance of developing testicular cancer was 2.15 times higher in the aviation group when compared to the nonaviation group (Table 3).

Table 2. USAF Active Duty Testicular Cancer Rates 1998-2008

Group	Cases	Population	Rate (per 100,000)
1998			
Aviators	3	14,497	20.7
Nonaviators	7	45,156	15.5
Total	10		
1999			
Aviators	1	14,324	7.0
Nonaviators	2	43,890	4.6
Total	3		
2000			
Aviators	4	14,160	28.2
Nonaviators	2	42,782	4.7
Total	6		
2001			
Aviators	1	13,629	7.3
Nonaviators	5	42,004	11.9
Total	6		
2002			
Aviators	2	13,026	15.4
Nonaviators	5	45,490	11.0
Total	7		
2003			
Aviators	5	13,537	36.9
Nonaviators	7	46,312	15.1
Total	12		
2004			
Aviators	5	13,519	37.0
Nonaviators	3	46,739	6.4
Total	8		
2005			
Aviators	0	13,383	0.0
Nonaviators	1	46,143	2.2
Total	1		
2006			
Aviators	0	12,681	0.0
Nonaviators	1	44,759	2.2
Total	1		
2007			
Aviators	3	12,458	24.1
Nonaviators	3	41,164	7.3
Total	6		
2008			
Aviators	1	12,757	7.8
Nonaviators	2	39,913	5.0
Total	3		
Total			
Aviators	25	147,971	16.9
Nonaviators	38	484,352	7.8
Total	63	632,323	10.0

Table 3. Testicular Cancer Risk in USAF Officer Aviators vs. Nonaviators

Group	Cancer		Total
	Yes	No	
Aviators	25	147,946	147,971
Nonaviators	38	484,314	484,352
Total	63	632,260	632,323

5.0 DISCUSSION

This study adds support to the previous studies that have indicated an increased risk of testicular cancer among military aviators when compared with their nonaviation counterparts. This study differs from the previous study in that it uses the ACTUR database to find cases of testicular cancer rather than using military hospital discharge data. The data in ACTUR should be more complete than just using hospital discharge data, especially as more and more USAF personnel are getting their specialty care at civilian facilities rather than at military hospitals. These cases would be included in the ACTUR database where they may have been missed using military hospital discharge data. This study differs from some of the studies that looked at cancer rates among civilian aviators. Not all of these found an increased rate of testicular cancer in the population of aviators, but they also used the general population for their comparison population. This may have led to an inaccurately elevated estimate of the risk because pilots and aircrew tend to be from a higher socioeconomic class than the general population, and it has been shown in the past that there is already a higher rate of testicular cancer among those from a higher socioeconomic class. This study controlled for that by using a comparison group that would be from a similar socioeconomic class.

While the odds ratio was elevated at 2.15, the 95% confidence interval crossed below 1.0 at the lower end. This indicated that the study did not have enough power to prove a significantly increased odds ratio. This does not mean that these results should be thrown out but just that further study with increased numbers of cases may need to be undertaken to confirm the elevated odds ratio. ACTUR is a great resource to obtain numerator data on cancers of all types reported in military beneficiaries. Including other branches of the military or even including the Air National Guard (ANG) or USAF Reserves could add additional cases and give the study more power. The ANG and USAF Reserve testicular cancer cases in the initial ACTUR data pull were not included in the analysis in this study because the denominator used to calculate the incidence rates did not include the ANG and USAF Reserve forces. While adding power to a study, one would need to use caution in including the ANG and USAF Reserve forces in the analysis because many of these individuals do not get their primary medical care from the military health care system, and they could conceivably be diagnosed with cancer and not included in the ACTUR database.

This study supports an association between being an aviator and an increased risk of developing testicular cancer. It does nothing to look at specific factors associated with being an aviator that may be contributing to the increased risk. Several factors have been suggested in the past as being occupational hazards that might contribute to the increased risk, including solar cosmic radiation, ultraviolet radiation, magnetic field exposure, and circadian rhythm issues. Further study is needed to determine what specific factors are causing the increased risk so that appropriate protective measures can be put in place.

One of the limitations with this study is that it combined all flyers together in one category. In the USAF, not all pilots have the same exposure parameters. A pilot flying on an intelligence, surveillance, and reconnaissance platform will have a different level of exposure to cosmic radiation than a pilot flying on a rotary wing (helicopter) platform. Also in this study there was quite a range of flying hours recorded by the aviators with testicular cancer. Further study needs to be done to see if there is a different rate of testicular cancer for those in certain airframes and with more time in the air. One would expect that the rate of testicular cancer would be higher in those with more hours, but you cannot make a statement about that one way or the other with the current study.

Another limitation of this study is that it assumes that all those who have reported flight hours were aviators at the time of diagnosis. Using the methods in this study, it is possible to be diagnosed with testicular cancer, get treated and cured, and then become an aviator; the case would have been counted as an aviator with cancer when, in fact, the cancer was diagnosed when the individual was not involved in aviation. This scenario would require a waiver, and the chance of it happening is small. It is more likely that an aviator was diagnosed with cancer, received treatment, and was granted a waiver to resume military flying duties. This would cause the number of flying hours to be inflated. A pilot could conceivably get diagnosed with cancer when he had relatively few flight hours and then go on and have a long career and log many additional flight hours. If you were to look at the risks of testicular cancer related to the number of flight hours, you would need to control for this factor.

One final limitation of this study that is consistent with the other studies of testicular cancer incidence is that it treats all testicular cancers the same. Testicular cancers come in many different types as described in the background section of this report. An environmental or occupational exposure may cause an increased incidence of one particular type of testicular cancer but not increase the incidence rate of other types. Once again, further study looking at the specific types of testicular cancer diagnosed would need to be performed to try to answer this question.

6.0 CONCLUSION

This study supports the previous indications that there is an association between military aviation status and the risk of being diagnosed with testicular cancer. Further study needs to be done to find if this result will reach the level of statistical and clinical significance. This study does not address the specific factors that may be contributing to this increased risk, and further study needs to be done to look for these factors that are contributing to this increased risk.

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LIST OF ABBREVIATIONS AND ACRONYMS

ACTUR	Automated Central Tumor Registry
AFPC	Air Force Personnel Center
AFSC	Air Force Specialty Code
DoD	Department of Defense
OR	odds ratio
RAW	Retrieval Application Website
RPI	Rated Position Identification
SIR	standardized incidence rate
USAF	United States Air Force